Strategic Straw Plan for Life Science SAXS

Prepared by Lin Yang

With input from Marc Allaire, Ben Hsiao, Hiro Tsurota, Tracy Nixon, Quan Hao

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Scope and Objectives

A wide variety of possible samples

molecules: proteins, RNAs

molecular assemblies: viruses, membrane structures, …

tissues: muscles, bones, …

• Support cutting-edge experiments that fully take advantage of NSLS-II source brightness

• Support experimental techniques the user community need the most.

Scientific needs: source-limited measurements

Time-resolved (~ms) measurements

Application: following the structural change of biomolecules in live biological processes. E.g. folding, complex formation, etc..

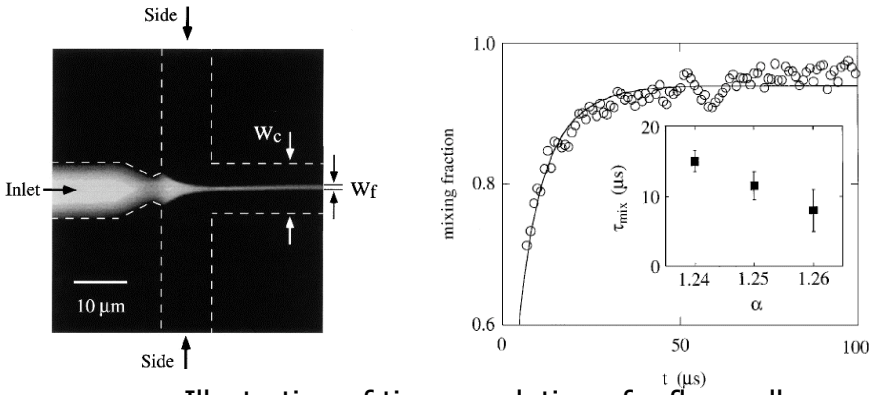


Illustration of time-resolution of a flow cell

Knight et.al., Phys. Rev. Lett., 1998

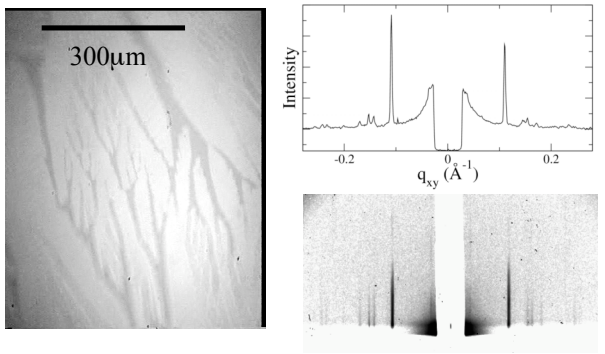
Comments and concerns:

Flow cell translates spatial resolution into time resolution. Smaller beamsize gives faster time resolution. Time resolution of ~10μs possible.

Sample consumption (several mg per data point) is a significant concern for life science users.

2D membrane structures

Application: structural study of membrane proteins in near-native membranes.



Diffraction from 2D crystals of Strepavidin

Fukuto et.al., on-going

Comments and concerns:

Measurements carried out in grazing incidence geometry. Require small beam footprint to achieve good angular resolution at large diffraction angles

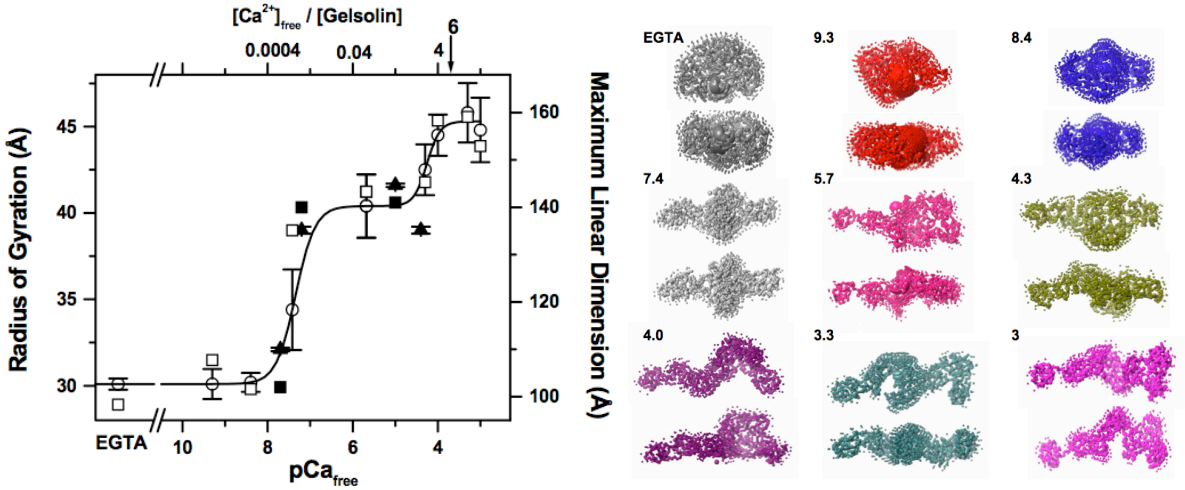
Other examples

Heterogeneous structures in biological tissues, bone (local structure may be interesting).

Scientific needs: sample-limited measurements

Scattering from biomolecules in solution

Application: low resolution structural characterization of biomolecules in solution.



Conformation change of Gelsolin as a function of free Ca concentration

Ashish et.al., J. Biol. Chem., 2007

Comments and concerns:

Protein solutions are more sensitive to radiation damage than protein crystals (as low as ~400Gy total dose, as compared to 10^7Gy). Possible dose rate dependence (faster damage at higher dose rate).

Data collection time is already short (seconds to a minute) even with existing sources. Rate limiting factor is sample turn-around, which also take seconds even with automated sample handling.

Other examples

Membrane structures in bulk (diffraction, also vulnerable to radiation damage, environmental control takes more time than measurements).

Current demand for life science SAXS

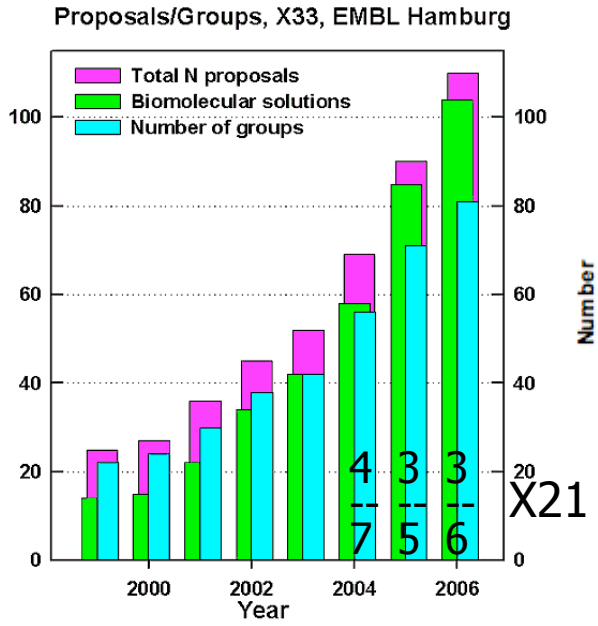
- time-resolved (ms) measurements, membrane structures, …

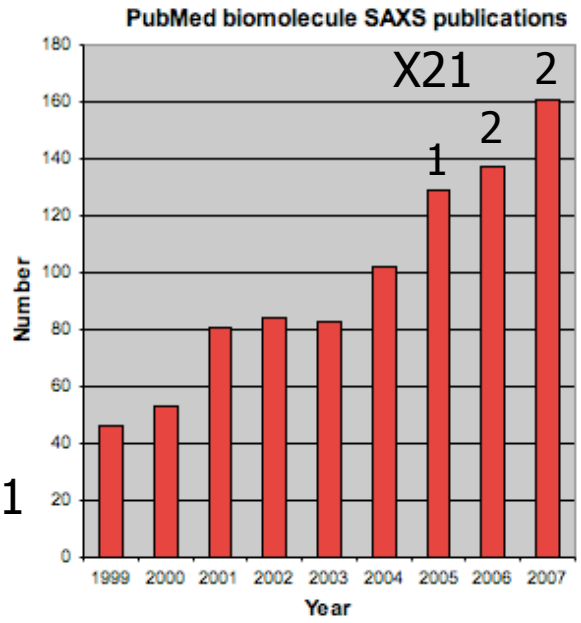
  Very few exploratory studies. May be categorized as soft condense matter / biophysics / biomaterials research rather than life science research.

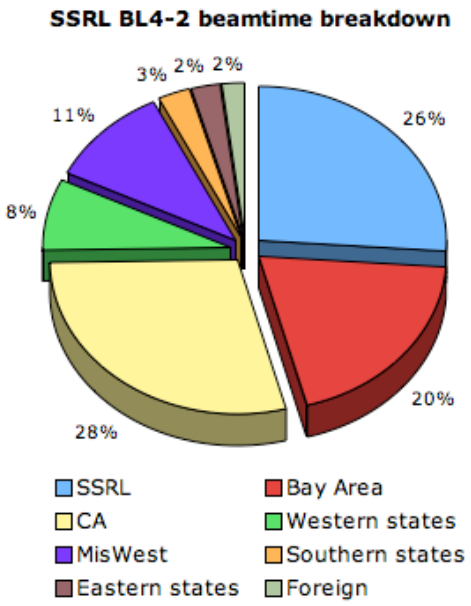
  Demand expected to increase because of new experiments enabled by the source brightness. But these experiments likely will not be able to occupy the full capacity of one beamline.

- solution scattering

  Rapidly increasing demand in past years. Number of publications also rising.







Life science SAXS beamlines at NSLS-II

ID beamline

- For experiments that need very high flux and very small beamsize.
- May not be able to occupy the full capacity of a beamline. Share with soft condensed matter community.
- Prefer an undulator source in a low-beta straight section (smaller source size).

3PW beamline

- For measurements that are already taking place at existing sources and anticipating increased demands, most notably solution scattering.
- Many of these measurements are limited by radiation damage to the sample and sample turn-around in measurements.
- Possible high throughput and mutil-probe (e.g. UV-Vis, IR and CD spectroscopy) capability to make better use of beamtime and samples.

Desired build-out plan:

1 3PW beamline dedicated to life science (solution scattering)

1 ID beamline shared with soft condensed matter / nano-science

1 3PW beamline shared with soft condensed matter / nano-science (fiber diffraction, multilayer membrane structures, …)

Existing NSLS SAXS beamlines and their movability

- X21 (wiggler)

  Fiber diffraction. Membrane structures.

  X21 is the only beamline currently supporting protein solution scattering. Also supports membrane structure experiments. Small but productive community.

  These capabilities will be moved to X9 at the end of FY08.

- X9 (MGU)

  Currently under construction. Bimorph KB mirror + cryo-cooled Si(111) mono with position feedback.

  Simultaneous SAXS/WAXS. Photon-counting pixel array detector.

  Flexible focusing schemes with micro-beam (10μm) capability, ideal for flowcell and membrane experiments.

  Suitable to be moved to NSLS-II.

- other beamlines (BM)

  Fiber diffraction from muscles and bones at X27C. PRT plans to move endstation to NSLS-II.

  Membrane structures (in bulk sample) at X6B.

X9

Detectors:

Princeton Instrument CCD.

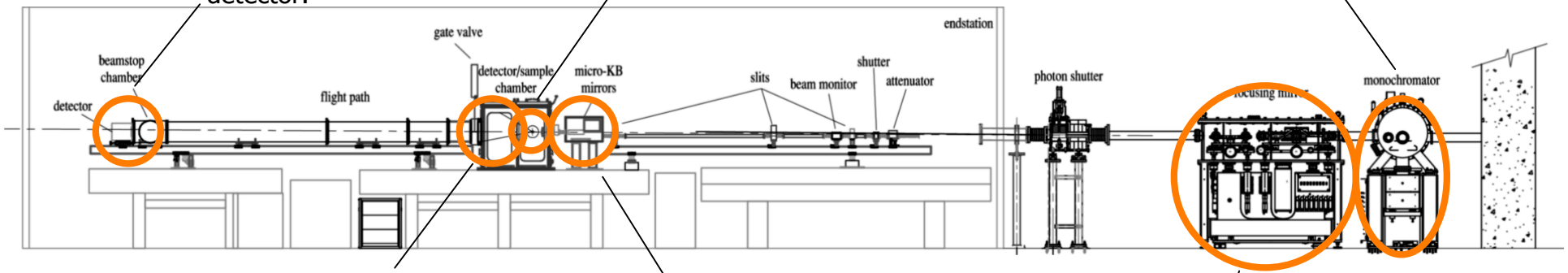
Dectris PILATUS pixel array detector.

Hexapod sample manipulator:

Ideal for measurements of 2D structures.

Si(111) mono:

With beam position feedback to enhance beam stability.



WAXS detector:

Customized Photonic Sicence CCD for simultaneous SAXS/WAXS data collection.

Micro-focusing KB pair:

Can create beam size down to 10μm using slits-defined secondary source.

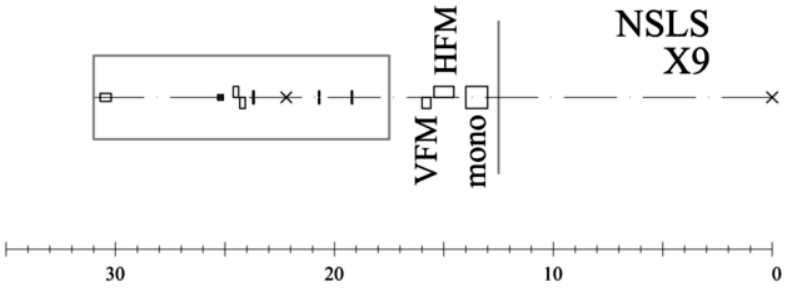
Bimorph KB focusing mirror pair:

Flexible focusing schemes.

NSLS-II ID beamline

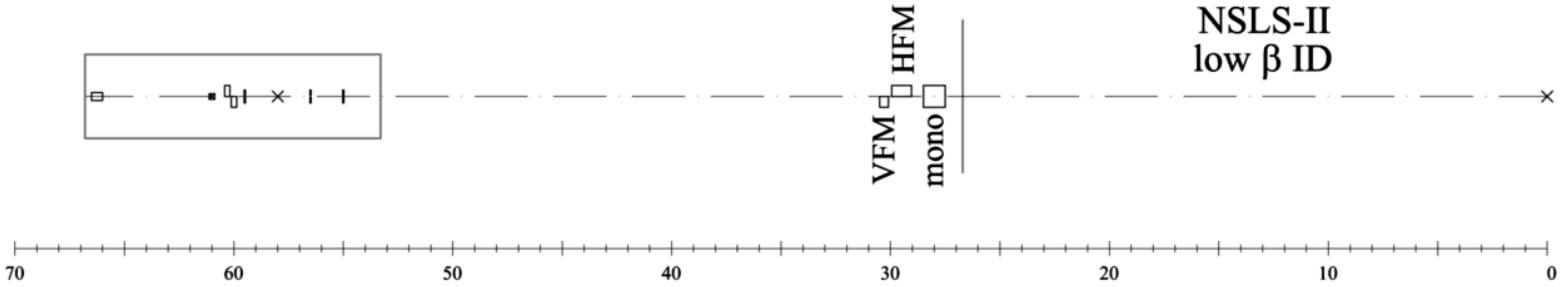
X9 suitable for moving to a U19 source at NSLS-II

- Endstation equipped to work with microbeam
- Designed for soft condensed matter / nano-science research.
- KB mirror will not work well on a 3PW or DW source (small optical aperture).
- Small source size (low beta) preferred.
- X9 mono designed to handle <100W heat load. >300W expected from U19.



0.8×10^{12} ph/s at the sample, 8keV, 0.01% bw

1.0×10^{14} ph/s at the sample, 8keV, 0.01% bw



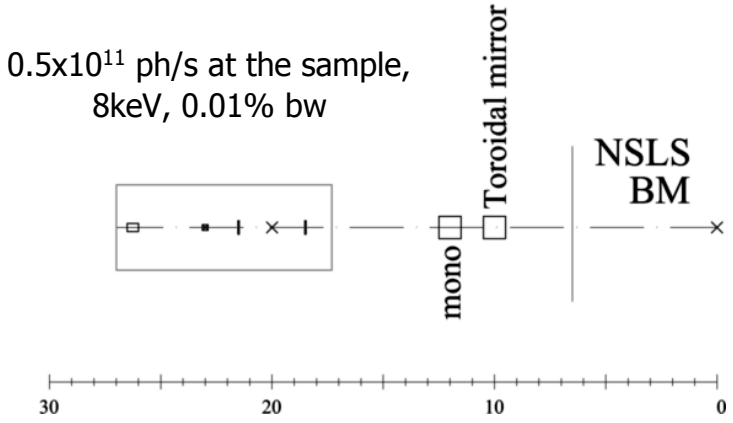
NSLS-II 3PW beamline

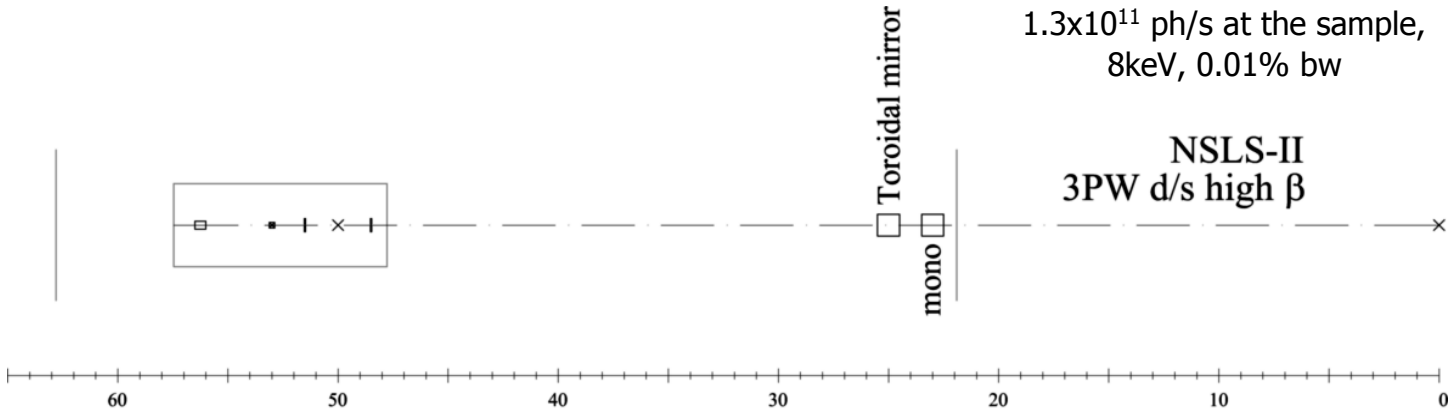
Dedicated solution scattering beamline to take over the community developed at X9

• Build up from scratch and operate from "day one" or before X9 is turned off.

• Comparable performance as a NSLS BM beamline. Use ML monochromator to boost flux.

• Possible to build a new beamline at NSLS then move (but desirable?).





User Support

- Instrumentation

  Combine multiple characterization tools with X-ray scattering:
  UV-Vis, IR, CD spectrocopy, DLS, … in-line with SAXS/WAXS measurements for protein solution samples
  Variety of optical microscopy in micro-beam measurements (bones, biological tissues)

  High throughput automatic sample handling for solution scattering.

- User service

  Need staff support for data analysis to attract novice users (compare to PX).

  Mail-in service.

- LOB facilities

  Protein expression, purification and characterization (important for samples that do not travel well / have poor stability).

Transition Plan

- User community development

  Very small user community right now. Need to attract experienced users and educate new users. Asked for NSLS-funded Post-doc for user support of solution scattering data analysis and mail-in service.

  NSLS operating budget-supported R&D of automatic sample handling.

  X9 will be hosting experiments in multiple scientific areas. Need commitment from NSLS management to support life science research, particularly solution scattering (e.g. guaranteed faction of beamtime at X9).

  Industry involvement (potential application for high throughput drug discovery).

- move to NSLS-II

  Seek funding for 3PW beamline (Need input from user community).

  Coordinate with soft condensed matter community on X9 transition. Seek MIE funding for undulator and new monochromator.

  Beamline transition funded by NSLS-II operating budget.